VI. Chemicals of Concern

A. Mercury

Methylmercury: Ongoing Research on Toxicology. Kathryn R. Mahaffey, US EPA

Fish and shellfish virtually all contain mercury, though both concentrations and consumption vary widely.

Key results to review here include the NRC 2000 report [2]; the US EPA's 2001 reference dose [17, 18]; biomonitoring measures; and current research findings.

EPA's 2001 RfD was based on a benchmark dose (BMDL) [19]. This was based on neuropsychological tests reflecting children's ability to learn and process information. Methyl mercury exposure doubled the risk of scores in a range considered subnormal. The BMDL that EPA used was based on doubling of the prevalence of scores in a range recognized as subnormal on tests of developmental function.

Biomarkers are used to represent exposure. One key issue is the relationship between mercury concentrations in umbilical cord blood in the developing child and in the mother.

Both US EPA and the National Academy of Sciences selected a BMDL of about $58~\mu g/L$ of mercury measured in the umbilical cord. The cord blood was assumed to have the same amount of mercury as the mother's blood. This is a common assumption.

More recent results suggest that this assumption may be incorrect and that cord blood is on average 1.7 times **higher** in mercury than maternal blood. This would mean that, if the level of mercury in the umbilical cord blood was 58 μ g/L, the level of mercury in the mother's blood would be expected to be about 34 μ g/L. The reasons for this difference are likely to be due to differences in the way the mercury is distributed and processed in the body of the mother and child. Differences in the mean ratio of cord blood to maternal blood varied in one study from 2.17 to 1.09 [20].

In developing the RfD, the uncertainty factors were set based on the assumption that the ratio was 1. This did not take account of this difference.

As noted in other talks, according to NHANES data, about 8% of women in the US exceed the EPA RfD of $5.8 \mu g/L$. The 90^{th} percentile is $4.84 \mu g/L$.

Effects of methylmercury in adults are also a concern. Are there cardiovascular effects in adults of low dose exposure to methyl mercury? Some results suggest that this may be the case. Salonen studied 1983 men living in Eastern Finland aged 42 to 60 years [21, 22]. This study reports that mercury is a risk factor for coronary and fatal cardiovascular disease. Dietary intake of fish and mercury were associated with significantly increased risk of acute myocardial infarction (AMI) and with death from coronary heart disease (CHD), cardiovascular disease and from any cause. Men in the highest tertile (2 ppm and higher hair mercury) had a 2-fold age- and CHD-adjusted risk of AMI (95% CI 1.2 to 3.1; P=0.005) and a 2.9-fold higher adjusted risk of cardiovascular death (95% CI, 1.2 to 6.6; P=0.014). This is a dramatic number.

Carotid intima-media thickness increased with increases in hair mercury concentration. This suggests that mercury accumulation in the human body is associated with accelerated progress of carotid atherosclerosis. This has been viewed as just one population. There is a multi center European trial on coronary heart disease that also measured heart disease, and results have been accepted for publication. Additional information should be available soon.

Setting a Methyl Mercury Reference Dose for Adults. Alan H. Stern, New Jersey Department of Environmental Protection

The policy of the U.S. EPA is to derive a single reference dose (RfD) per chemical based on goal of protecting most sensitive group. Generally, members of the sensitive group are not known, or cannot control their exposure (e.g., air or drinking water). Therefore, protection of sensitive groups results in overprotection of general population.

However, for methyl mercury (MeHg), the sensitive population is well characterized and is women of childbearing age, pregnant women, and young children. Individuals have reasonable control over exposure in that they control their fish consumption. They can consume fish with lower mercury concentrations, at least in theory.

In principle, this lends itself to a two-tiered advisory structure for the sensitive population and general population. The general population is not overly protected and has less potential limitations on obtaining nutritional value from fish. The sensitive population is protected at more stringent level.

The two-tiered approach is based on two RfDs. The current RfD is based on neurodevelopmental effects for the sensitive population.

The previous RfD, which is applied to the general population, is based on neurological effects for general population and is specifically protective against the occurrence of paraesthesia. This was the basis for the previous US EPA methyl mercury RfD, which was based on studies from Iraq ¹ and Minamata. It is appropriate to consider whether this is still an appropriate endpoint when more subtle health endpoints are considered.

Currently, 12-13 states follow a two-tiered approach. The appropriateness of this approach is predicated on the assumption that the reference dose for the general population will be less than that for a sensitive population (Rfd_{gen} > RfD_{sens}). The current RfD is 0.1 μ g/kg/day, while the old RfD (for the general population) was 0.3 μ g/kg/day. This difference is small, but significant for fish advisories and allows for two different consumption rates for fish advisories.

Is the assumption that the RfD for the general population will be greater than the RfD for the sensitive population (Rfd_{gen} > RfD_{sens}) correct? The NRC report highlights several areas of uncertainty for a general ("adult") RfD, particularly cardiovascular effects and immunotoxic effects [2]. Currently lacking is a lifetime exposure assessment that addresses in *utero* plus adult exposures, as effects may be due to the combination of developmental as well as adult-stage health impacts.

The NRC committee felt that there was not enough information in the literature or enough time to peer review all of the studies that were available and to derive reference dose for these endpoints. Their recommendation was to add an uncertainty factor of 3 (half a log unit) to deal with this, for database uncertainties related to adult effects.

Researchers have reported some findings for cardiovascular endpoints for MeHg. Salonen et al. [22] looked at middle aged Finnish men. The mean hair mercury was 1.92 ppm, approximately 2.3 times the New Jersey general population mean. For men with hair mercury greater than 2 ppm, the adjusted relative risk for AMI, CHD, and CVD were 1.7 to 2.1. In New Jersey, about 20% of general population has hair concentrations greater than 2 ppm.

The Salonen study [21] included a 4 year follow-up assessing hair Hg, and atherosclerosis progression. They used ultrasound determination of carotid artery thickness, which is a major advance in assessing pre-clinical effects. After adjustment for co-variates, men in upper quintile of hair mercury (2.8 ppm in hair) had a 40% increase in arterial wall thickness.

If the RfD for the general population is higher than the RfD for sensitive populations, we would retain the two tier structure. Currently they are separated by only $0.2~\mu g/kg/day$. If the RfD for the general population decreases by $0.1~\mu g/kg/day$, will the difference in advisories be significant? If the RfD for the general population is lower than that for the "sensitive" populations, would we just have one advisory? Does the cardiovascular endpoint apply to women?

EPA has sponsored a project to look at these issues, to be investigated by Dr. Alan H. Stern with Dr. Andy E. Smith of Maine as the co-principal investigator. Other participants include state toxicologists, epidemiologists, risk assessors. The project will also include independent consultants in statistics and cardio-epidemiology.

Note: Dr. Stern was a member of the NRC panel.

Henry Anderson, Wisconsin: Because of benefits of fish consumption, maybe you would want to call this something other than an RfD?

Response: Any integrated analysis that looks at mercury exposure and health effects should integrate competing processes of beneficial omega three fatty acids. The trick is to see to what extent this is actually occurring. Another paper suggests that when mercury is present, benefits of omega three fatty acids are lost.

Kate Mahaffey: There is a big literature about omega 3 and omega 6 in various fish. They are associated with fat in fish. We can have fish that are high in omega 3's but not high in mercury. It is misleading to think that just because you select fish lower in mercury that you are winding up with fish lower in these fatty acids.

Andy Smith: this will be addressed by a speaker on the fish oils issues

Kate Mahaffey: Going from the benchmark dose (BMDL) to the reference dose has an uncertainty factor of ten, which has several components, but it assumed that cord blood and maternal blood are equal. Some of this factor is eroded by what we know so far.

Deb Rice: The NAS panel used the critical study/critical endpoint approach to choose a point of departure for calculating an RfD, in accordance with typical practice. They chose the Faroe Islands study as the critical study, and the Boston Naming Test as the critical endpoint. However, they also performed an integrative analysis of all three studies combined, to encourage better use of all the available data. EPA considered the RfD to be based on a number of endpoints from the Faroe Islands and New Zealand studies, as well as the integrative analysis. Most of these endpoints yield an RfD of 0.1 µg/kg/day. The BMDL from the Boston Naming Test is 58 ppm in blood; however, any one of a number of other endpoints could have been chosen as representative of the RfD. For example, the BMDL for the integrative analysis is 32 µg/kg/day.

Alan Stern: They did an integrated analysis in a less formal sense with the Faroe Islands data. I agree with you. The intent on the committee was to come up with the test that gave the lowest BMDL that was clearly defensible. They did not pick the lowest one, which was the continuous performance test, but the test giving the most sensitive mercury effect (the Boston naming test) because they thought it was a more robust test. 58 µg/kg/day was one of several numbers within a fairly narrow range that could have been chosen, but it was not the lowest number that could have been shown.

B. Brominated Flame Retardants

Occurrence of PBDE Flame Retardants in Fish. Robert C. Hale, Virginia Institute of Marine Science

The term "brominated flame retardants" is often used interchangeably with "polybrominated diphenyl ethers." In reality, PBDEs are a subclass of BFRs, which are chemicals added to products up to reduce fire hazards. Products can contain up to 30% of them by weight.

BFRs have differing chemical structures. However, PBDEs and PBBs (poly brominated biphenyls) have very similar chemical structures, which differ only in that the PBDEs have an ether linkage not found in the PBBs. Both resemble the highly toxic and persistent PCBs.

In 1973, PBBs were inadvertently introduced into livestock feed in Michigan and subsequently into people. As a result, a large number of animals had to be destroyed, but many people still carry body burdens. Following this incident, PBB use in the US was suspended.

There are three commercial PBDE mixtures now in use in the US, referred to as "Deca," "Penta," and "Octa." Deca-BDE is used in thermoplastics and textiles. Penta BDE is used in polyurethane foam, and Americans use 98% of the world's total production. Octa-BDE is less common and mostly used in thermoplastics. They are mixtures that are numbered just like PCB congeners.

These mixtures consist of individual congeners, which have been assigned numbers like PCB congeners, to reflect the number of halogens and their position.

Deca (BDE-209) strongly partitions to sediments and does not represent as much of a bioconcentration hazard as some other forms. The congeners that comprise the "Penta" product tend to partition similarly to PCBs. Bioaccumulation is high and probably occurs to a greater degree for these compounds than for PCBs.

PBDEs are resistant to environmental degradation and subject to long range transport. Those with less than seven bromines have higher vapor pressure and appear to be subject to long range transport. Accumulation in fish is a major pathway for human exposure, as per PCBs.

European researchers have conducted more research in this area than researchers in the US. Their work suggests that the less brominated congeners have already reached remote areas.

Levels in breast milk measured in North America are increasing logarithmically, in proportion to our relatively higher use.

The European Union has issued a ban on the penta mixes, scheduled to go into effect in 2003.

It has been suggested that Deca (BDE-209) may be vulnerable to debromination in some conditions, perhaps including the presence of UV light. However, there is no currently published literature showing that degradation of BDE-209 is responsible for the distribution of tetra- and penta-brominated congeners in the environment.

To date, the US has no regulations restricting the use or disposal of these compounds.

The Mussel Watch program (which routinely monitors concentrations of contaminants in sediments and shellfish) is expected to add the PBDEs to its surveillance program.

The first documentation of PBDE concentrations in North American aquatic organisms was from 1987 and reported about 200 ppb in lipids of dolphins. Marine mammals seem to be very high accumulators. Levels in San Francisco Bay seals increased 65-fold from 1988 to 2000 [23]. The values in the US are increasing over time, and tetra-brominated compounds are being found in virtually all samples.

A case study from Virginia, published in Environmental Science and Technology, was conducted in 1998-9 in the Roanoke Basin [24]. It found BDE-47, the most commonly reported congener and a major component of the Penta- mixture, in 89% of Roanoke basin fish fillets. Other congeners were present as well. The detection of PBDEs in rivers surrounded by dams debunks the idea that it comes from historical uses of drilling muds or marine sponges. Sources are likely to be local. There is a history of textile mill and furniture manufacturers in the area. While there is some statistical correlation between PCBs and PBDE concentrations, there were also outliers. This suggests that the original sources may differ.

Major PBDE commercial products in use in North America in 1999.

Commercial PBDE Mixture	1999 North American demand (tons)	Percent of 1999 Global Demand	Major component PBDE congeners
Penta-	8290	97.5%	BDE-47, 99, 100, 153, 154, 85
Octa-	1375	35.9%	BDE-183, 153, unknown octa- and nona-BDEs
Deca-	24300	44.3%	BDE-209, unknown nona-BDEs
Total	33965	50.6%	

PBDEs: Toxicology and Human Exposure.

Linda S. Birnbaum, US Environmental Protection Agency

The brominated flame retardants are major industrial products (~67 metric tons/year). There are several forms.

The "deca" compounds are produced in the largest volume (75% of what is produced in the European Union.) They are used in polymers, electronic equipment, and textiles.

The "octa" compounds are used as polymers, especially in office equipment.

The PeBDEs are most problematic. They are used in textiles and polyurethane foams (up to 30%). A ban has been recommended in the European Union for these compounds, allowing no production, only import. Essentially they are not being used except in North America

The mixes of congeners vary by medium.

In air: 47>99>100>153=154.

The pattern in sludge looks like the pattern in foam, as you see less 47 than 99.

In sediments, concentrations of congener 99 are higher than 47. This pattern reflects commercial PeBDEs along with some also some nona and deca forms.

In biota, 47>99=100 except in locations near a manufacturing site. This pattern does not reflect commercial mixtures. In a commercial mixture you have more 99 than 47

For concentrations in biota, marine mammals have much higher concentrations than other organisms. Fish are lower and invertebrates about the same or slightly lower.

For ecotoxicity, PeBDEs are much worse than OBDEs which are worse than DBDEs. They are highly toxic to invertebrates (For larval development, the lethal effects levels are in the low μ g/L range.)

DBDEs and OBDEs may be low risk to surface water organisms and top predators. There are concerns for waste water, sediment, and soil organisms. The presence of lower brominated congeners in OBDE, which could lead to penta forms, is a concern. Photolytic and/or anaerobic debromination can also give us penta forms.

For mammals, concerns are liver effects, enzyme induction. DBDE is a hepatocarcinogen at high doses. There are also neurotoxic effects. More recent studies show more subtle effects. Changes seen would be associated with learning issues in adults and could lead to permanent changes in brain function. Moreover, developmental exposure may lead to increased susceptibility of adults exposed to low doses of PBDEs. *In vitro* studies show changes in signaling pathways

Endocrine disrupting effects include AhR effects, thyroid effects, and estrogenic effects. For thyroid the real concern has to do with ability to disrupt thyroid homeostasis. Some forms are estrogenic.

PBDEs are readily absorbed except for DBDE, which is poorly absorbed. Lipid binding is important. In fat, 47>99>>>209. In the liver, you see covalent binding from 99 and 209. Metabolism is through hydroxylation, debromination, and O-methylation. Excretion is primarily in feces.

Trends of BDEs in human milk pose an important concern. In Sweden, results show an exponential rise that peaked in about 1997 and then went down after they stopped using it in 1994. Levels in Europe are much lower than what we are starting to see here in North America; levels of use are 10 times higher here than there and they have stopped using the penta formulation. Our levels are much higher; some people are far above the range of any other people and highly exposed.

Total BDEs in contemporary human milk (ng/g lipid) [25]

Country	Number of samples	Year	Median	Mean
Sweden	93	1996-1999	3.2	4.0
Japan	12	2000?	1.4	1.3
Canada	50	2001-02	25	64
USA (adipose)	23	1998	41	86

Measurements of PBDEs in human samples in the US [23] show that 47 is about 40% of total; 153 is about 20%, 154 is about 17% and 99 and 100 are about 10%. There is little 99 compared to what is present in a commercial mixture. Possible explanations are that these may be more persistent or perhaps they are coming from octa mixtures or debromination of deca mixtures. The mix measured is totally unlike the original formulation of the products.

Though limited data are available, it appears that concentrations have increased dramatically in measurements made in California.

Fig. 2 PBDE 47 in California women

Source: [26]

Measurements made in Canada show that the sum of eight congeners in breast milk has increased greatly since around 1992 and is largely driven by 47. The pattern of congeners is different from commercial mixtures (and food). In the US and Europe, 47 is higher than 99 (others: 100, 153, 183, and 209?). In Japan, 99 and 153 are higher than 47. There are also large interindividual differences.

Concentrations are doubling every 2-5 years. PBDE and PCB levels are not correlated. In most samples today, PCBs are greater than PBDEs. There are likely to be different sources and/or a different time sequence.

The key question is whether levels are high enough to see effects. To determine this, we need more toxicology data. We also need:

- More systematic human and environmental monitoring;
- More information on fate and transport are commercial products breaking down? And into what?
- More toxicology data that focus on congeners present in people and wildlife, not commercial products since they are altered in the environment.

Polybrominated Diphenyl Ethers (BDEs). Khizar Wasti, Virginia Department of Health

In view of BDES being detected in fish at 1-2 milligrams per kilogram (mg/kg) range, the state of Virginia developed guidance levels for the issuance of a fish consumption advisory for BDEs. To date, information available in the literature regarding the toxicity of BDEs is very limited.

For deca-BDE, the acute toxicity in experimental animals is low. The oral LD50 in rats is greater than 5 mg/kg. No adverse effects were noted in rats fed at doses of up to 800 mg/kg body weight for 30 days. There is no evidence of carcinogenic, reproductive, teratogenic, or mutagenic effects. Epidemiological studies in occupationally exposed workers did not indicate any symptoms attributable to BDE exposure. In the U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) database, the oral reference dose (RfD) is reported as 0.01 mg/kg/day.

For octa-BDE, the acute toxicity in experimental animals is low. The oral LD50 in rats is greater than 5,000 to 28,000 mg/kg. Teratogenicity was seen at doses of 25 and 50 mg/kg body weight; resorptions or delayed ossification of different bones and fetal malformations were noted in rats. These changes were not seen at 15 mg/kg dose or less. In rabbits there was no teratogenicity, but fetotoxicity was seen at a maternally toxic dose of 15 mg/kg. A no-effect level was 2.5 mg/kg. Assays for mutagenicity were negative. For carcinogenicity, no data are available to date. The oral RfD in the IRIS database is reported to be 0.003 mg/kg/day.

For penta-BDE, acute oral toxicity is low with an LD50 in rats of 6,000 to 7,000 mg/kg. Rats given a diet containing 100 mg/kg for 90 days showed no clinical effects. It was not found to be mutagenic, and there are no data on its carcinogenicity. In the IRIS Database, the oral RfD is reported as 0.002 mg/kg/day.

For tetra-BDE, no human or animal data are available. Toxicity may be assumed to be similar to commercial penta-BDE since it contains significant amount of tetra-isomer.

Since very little toxicity information was available in the literature, Virginia sought assistance from various federal and state agencies. A task force was formed comprising staff from health and environmental agencies in Virginia and North Carolina, and two federal agencies which included EPA and the Centers for Disease Control and Prevention (CDC). To derive an allowable BDE level in fish, the oral RfD values of penta-isomer (0.002 mg/kg/day); octa-isomer (0.003 mg/kg/day); and deca-isomer (0.01 mg/kg/day) were compared. The task force members concurred with the approach of selecting the RfD of the most toxic isomer to be used in deriving guidance levels for BDEs in fish. The task force considered the option of using the RfD value for penta-isomer, 0.002 mg/kg/day. EPA suggested using an interim RfD for tetra-isomer, 0.001 mg/kg/day. This RfD value was based on the assumption that tetra-BDE is twice as toxic as the penta-isomer. Virginia used this RfD and a consumption rate of two 8-ounce meals per month to derive a trigger level for the issuance of a fish consumption advisory.

The equation used for deriving the trigger level is as follows:

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\underline{0.001 \text{ mg/kg/day} \times 70 \text{ kg} \times 30 \text{ days/month}} = 4.62 ~ 5.0 mg/kg or parts per million (ppm) 0.227 kg/meal x 2 meals/month
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Using this equation, the allowable meals per month at various BDE concentrations can be calculated and are shown in the table.

Concentration (mg/kg or ppm)	# of Meals per month
1	9.3
1.47	6.3
2	4.6
3	3.1
4	2.3
5	1.9
9	1
10	0.9

Based on the calculations above, Virginia uses the following trigger levels for the issuance of a fish consumption advisory when fish is contaminated with BDEs.

- Below 5 mg/kg or ppm no advisory
- 5 to below 10 mg/kg or ppm two eight ounce meals per month
- Above 10 mg/kg or ppm no consumption

Because data are limited and reproductive or developmental effects of BDEs have not yet been evaluated, the state concluded that it would be prudent for pregnant women, nursing mothers, and young children to avoid consumption of fish contaminated with BDEs above 5 mg/kg or ppm. Since reported concentrations in fish were below the trigger level, no advisory was issued. In issuing advisories Virginia tries to give the message that not every concentration is harmful.

Gary Ginsburg: Given the similarities between these compounds and PBBs, did you look at toxicological data for PCBs?

Response: There was no information on PBBs either.

Luanne: This was one reason EPA recommended an additional safety factor of 2. New RfDs are pending

Linda Birnbaum: If neurodevelopmental effects were addressed, it would lower the number by three orders of magnitude.

C. Dioxins and Coplanar PCBs

*Emerging Science of the Dioxin Reassessment.*Dwain Winters, US EPA

A number of things have happened with the US EPA's reassessment of dioxin assessment in the last year.

Dioxin-like compounds include dioxins, furans and PCBs. There are 75 dioxin congeners, and we consider seven of them to be highly toxic. There are 135 furan congeners, and we consider 10 of them to be highly toxic. There are 209 PCB congeners and we consider 12 to be highly toxic.

We use TEQs to compare congeners of different toxicity. (The TEQs reflects the relative toxicity of each congener.) These are fundamental to the evaluation of these compounds. They are based on multiple endpoints or on the binding of the compound to a receptor. The TEQs developed by the World Health Organization are accepted internationally and have the most comprehensive discussion.

Five compounds make up about 80% of the total TEQ in human tissues. Four of these are dioxin/furan compounds and one is a PCB. They are: 2,3,7,9-TCDD, 1,2,3,7,8-PCDD, 1,2,3,6,7,8-HxCDD, 2,3,4,7,8-PCDF, and PCB 126.

The current human exposure to dioxin TEQ for adults in the US is about 1 pg TEQ/kg/d (one picogram of dioxin TEQ per kilogram of body weight per day). Populations that may have higher intake include nursing infants, people with a fatty diet, subsistence fishers, and farmers in proximity to contamination.

EPA has concluded that for dioxin, unlike many other chemicals, the body burden is the best dose metric. It accounts for differences in half life and results in strong agreement between human and animal data. This approach has been adopted by the World Health Organization, European Union, and the US. The metric is ng/kg BW (nanograms of dioxin TEQ per kilogram of body weight.)

2,3,7,8-TCDD is considered to be a known carcinogen for humans, while other dioxin-like compounds and complex environmental mixtures of these compounds are considered likely to be carcinogenic. This based on unequivocal animal data studies demonstrating carcinogenicity and limited human studies.

Cancer potency estimates are primarily based on recently published human epidemiological studies. EPA's potency value has been revised upward by a factor of six compared to a value published by EPA in 1985 based on a rat study. Cancer risks to the general population may

exceed 1 per 1,000 from normal (dietary) exposure. This is not the upper bound, though risks may be less.

Non-cancer toxic effects of concern include developmental toxicity (affecting the immune system, nervous system and reproductive system), immunotoxicity, endocrine effects, chloracne and others.

Information about non-cancer effects in animals and humans is sufficient to generate a level of concern similar to that for cancer. It is likely that part of the general population is at or near exposure levels where adverse effects can be anticipated.

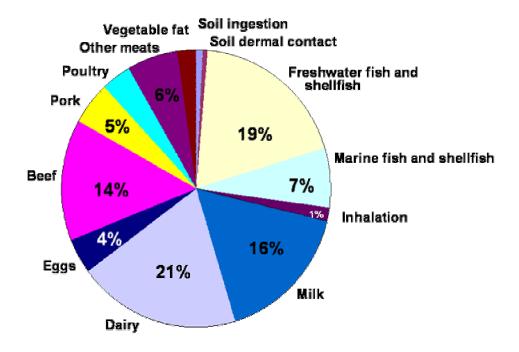
This table summarizes the body burdens associated with adverse effects. The margins between current average body burden (5 nanograms per kilogram - ng/kg) and these effect levels are mostly less than an order of magnitude, so some people are at levels likely to result in adverse effects. Consequently, EPA will not develop an RfD for dioxin.

Adverse Effects Body Burden (Ng/Kg) Developmental neurotoxicity: 22 Developmental/reproductive toxicity: 0.7 - 42Developmental immunotoxicity: 50 Adult immunotoxicity: 1.6 - 12 **Endometriosis:** 22 **Biochemical Effects** 0.6 - 33CYP1A1 Induction: 2.1 - 83CYP1A2 Induction

Most exposure is from the diet, but no one component dominates. Statistically based surveys of beef, pork, and poultry were done in 1994-95 and 1996-97. These are being re-sampled now, so some time trend data will be available. Fish data are more problematic because they do not lend themselves to statistical analysis. EPA is compiling data on dioxins in fish and welcomes submittal of relevant data.

Pathways for dioxin exposure include ingestion of soil, meats, dairy products, and fish; inhalation of vapors and particulates; and dermal contact with the soil. Sources include combustion, metals processing, chemical manufacturing, biological and photochemical processes, and reservoir sources.

The sources of US adult daily intake of dioxins, furans, and dioxin-like PCBs are shown in this chart.



The sources and pathways involve discharges to air and water, transport through the air, deposition from the air, and re-entrainment to soil particles. The compounds bind to leaves that are consumed and then get into food supply.

Releases have been greatly reduced in the last ten years. Municipal and medical waste incinerators have been greatly reduced. A major source remains backyard barrel burning. Some sources are poorly characterized. Reservoir sources are past releases of dioxin that are "stored" in the environment but that can be reintroduced. About 50% of population exposure is related to these sources. Most incorporation into food supply is in the corn belt, dairy states, and west. These are mostly upwind from major emission sources. Major reductions in emissions will not see proportional reduction in exposure because we are looking at complex exchanges between compartments. These need to be better understood.

D. Lead

Application of the Lead IEUBK Model to Assess Spokane River Fish Consumption Risks. Lon Kissinger, US EPA

The Spokane River is down river from the Bunker Hill Superfund Site and the Coeur d'Alene mining district, which are sources of lead in Idaho.

The goal of the project was to assess lead risks and develop fish advisories using models that predict blood lead concentrations. Such approaches integrate lead risk for all exposure routes. Two models were used. The first model, the Integrated Exposure Uptake Biokinetic Model (IEUBK) assesses risk for children age 0 to 84 months. The IEUBK model output is a probability distribution of blood lead concentrations. EPA currently uses a criterion that lead

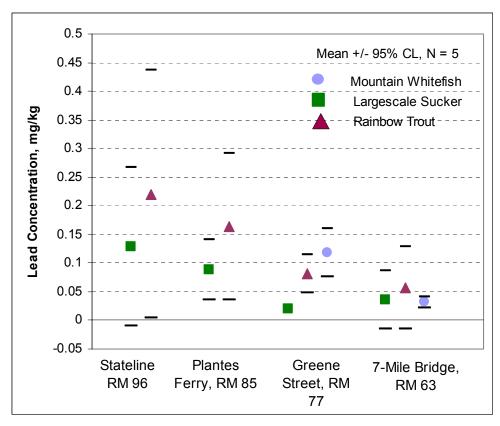
risks are tolerable if no more than 5% of predicted blood lead concentrations exceed 10 micrograms per deciliter (ug/dL). The 10 microgram per deciliter cutoff is supported by the CDC. The second model, the adult lead model, is used to assess risks to the developing fetus. This model assumes that if you maintain the mother's blood lead level within an acceptable range, then the risks to the developing fetus will be tolerable.

Information on the models is available at EPA's Lead Technical Review Workgroup web site: http://www.epa.gov/superfund/programs/lead/

The IEUBK model, as used for the assessment of lead risks from Spokane River fish, incorporates a number of parameters, which include the fraction of meat consumption that consists of locally caught fish, the concentration of lead in fish tissue, and lead concentrations and intake rates for other media. Fish tissue and sediments were sampled and analyzed for lead at a number of locations. In general, fish tissue and sediment lead concentrations were positively correlated.

One issue for this study was that there were no site specific, quantitative information about fish consumption for children. In the absence of such data, a children's tribal fish consumption rate, developed by the Columbia River Intertribal Fish Commission, was used. The 65th percentile consumption rate of 16.2 grams per day was considered to be health protective.

Spokane River Fish Fillet Lead Concentrations



Species tested for lead included mountain whitefish, largescale sucker, and rainbow trout. The mean levels in rainbow trout were 0.82 mg/kg and in largescale sucker 2.8 mg/kg. These levels were substantially higher than background values in fish (Schmitt and Brumbaugh, 1990.) Whole fish had much higher lead concentrations than filets.

IEUBK parameter values were: a state line trout fillet lead concentration of 0.22 mg/kg; a soil concentration of 230 mg/kg; other parameters at model defaults.

The model predicted that 3.7% of children consuming fillets would have blood lead levels above $10 \mu g/dL$. This was less than 5%, so the risk was judged to be tolerable.

For those who ate whole fish, the percentage exceeding $10 \mu g/dl$ was much higher. Using the maximum observed lead concentration, 62% would be above a blood lead level of $10 \mu g/dl$ if they consumed whole large scale sucker; 15% for rainbow trout; and 6% for mountain whitefish.

The model results were used to compute meal limits for children and adults. The results can also be used to see the effect of percent of meat consumed as fish.

In employing the IEUBK model to assess lead fish consumption risks, it is important to take soil lead exposure into account. High soil lead exposures will reduce the allowable levels in fish.

Editor's note: There is no known safe exposure to lead and effects have been found for children with blood lead concentrations below $10 \mu g/dL$.

Occurrence of Lead in Fish: Examples from Georgia, Maine, and California. Robert K. Brodberg, California Environmental Protection Agency

Lead has not been widely monitored in fish advisory programs. It is not one of the target analytes recommended by U.S. EPA to assess chemical contaminants in fish [27]. A few advisories have been issued for lead contamination in fish. Is there evidence that lead bioaccumulation in fish is a problem that is being missed due to lack of monitoring? This presentation summarizes preliminary data from Georgia, Maine, and California showing the occurrence of lead in sport fish in these states. Randy Manning summarized data from Georgia and Eric Frohmberg contributed the data from Maine.

Georgia

Georgia summarizes its monitoring data by water basin and hydrologic unit. Over 1700 fish fillet samples have been analyzed for lead using a detection limit of 1 ppm. Lead above 1 ppm has only been detected in about 4% of the samples. Lead has been detected most often in largemouth bass and channel catfish. It has also been detected in hog suckers, trout and sunfish. The highest levels have been found in the Upper Ocmulgee hydrologic unit (largemouth bass, 11.5 ppm; channel catfish, 15.5 ppm). This could indicate that there is a regional source of lead in this area. Or, it might indicate a local problem with clean preparation techniques or crosscontamination because samples are prepared in local jurisdictions. In either case, closer investigation is warranted.

Maine

Maine's summary of lead data includes over 300 fish samples. Maine used a lower detection level (0.02-0.05 ppm), and lead was detected in about 70% of the samples. The average lead

concentration in these samples was between 0.05 and 0.6 ppm. In only one case did the average lead concentration exceed the Maine action level of 0.6 ppm. Maximum values in some fillet samples of brook trout and smallmouth bass reached about 1 ppm. Lead concentrations in whole fish samples were generally low with the exception of white sucker (maximum concentration about 0.7 ppm), which has intramuscular bones. Some data were available to compare lead concentrations in the same species, prepared and analyzed whole body versus as fillets. Brook trout and smallmouth bass had higher concentrations in fillet samples than in whole body samples. However, lead concentrations in fillet and whole body samples of landlocked salmon and white perch were about equal.

California

In California, lead measurements were available for about 250 composite fillet, whole body or liver samples from the Toxic Substances Monitoring Program. The lead concentration in greater than 80% of all samples was less than the detection limit (0.001 ppm). Levels in whole body samples (maximum concentration 0.5 ppm) tended to be higher than in fillet samples (maximum concentration 0.2 ppm). The highest lead concentration was measured in white croaker liver. Overall there was not a noticeable difference in concentrations between inland and marine species.

Conclusions

Lead concentrations in sport fish varied between the states. Comparison is limited by differences in methods and detection limits, but the data show that a potential for bioaccumulation exists. Still, in most cases, results were below the Maine action level (0.6 ppm), and many samples were at or below detection limits.

This limited summary suggests that while lead may bioaccumulate in fish, it is not accumulating to levels that indicate a wide-spread problem. Nonetheless, screening level monitoring should be considered in areas of known or suspected high lead contamination.

One potential problem that should be considered when sampling fish for lead bioaccumulation is internal and external contamination. In a study of fish from streams in the Missouri lead belt, Schmitt and Finger [28] showed that differences in preparation can result in up to a ten fold difference in lead concentrations. Most laboratories now use "clean metal" techniques, which reduce external contamination. However, additional caution is needed because lead can accumulate in bone, scales and skin (e.g., by adhering to the skin surface). This might account for cases in which whole fish show higher lead concentration than fillet samples. And this can increase the apparent concentration in fish with intramuscular bones that are not removed in fillets. Lead can also be introduced from scales, skin and mucus, especially during field preparations. Differential inclusion of these non-muscle sources can also increase sample heterogeneity and consequently variation in reported lead concentration.

E. Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic Aromatic Hydrocarbons (PAHs) in Fish and Invertebrates. Usha Varanasi, National Oceanic and Atmospheric Administration

Polycyclic aromatic hydrocarbons (PAHs) are toxic compounds that are released from a variety of natural (e.g., oil seeps and fires) and anthropogenic (e.g., oil spills, combustion engines, coal burning, and wood preservative) sources. PAHs enter our nation's waterways and oceans through both point and non-point mechanisms, exposing valuable fish and invertebrate resources to toxic PAH compounds.

Once fish and invertebrates are exposed to PAHs, they readily absorb the compounds into their bodies. Key questions then become "is seafood safe to eat?" and "are there adverse effects on the organisms?" The answers for these questions are different for fish and invertebrates.

Vertebrates, including fish, metabolize (body processes that transform substances) PAHs quickly and efficiently in their liver to detoxify their systems. They readily convert most hydrocarbons to metabolites that are eliminated into bile and out of their bodies. High molecular weight PAH compounds, however, can be converted to reactive intermediates that bind to intracellular targets (e.g., DNA) and alter their function. Because vertebrates metabolize PAHs so quickly and efficiently, very little toxic product is found in their edible tissues; however, toxic products and byproducts can have a number of adverse effects on the fish themselves.

Invertebrates (e.g., mollusks and crabs), on the other hand, metabolize PAHs slowly and inefficiently (or not at all); they are unable to readily convert hydrocarbons to metabolites and eliminate them from their bodies. Because invertebrates metabolize PAHs so slowly and inefficiently, they accumulate toxic PAH compounds in their tissues, which can cause acute effects to the organisms, as well as a seafood safety concern.

PAH compounds are fluorescent, enabling scientists to screen for them using high pressure liquid chromatography or Gas Chromatography/Mass Spectrometry analysis. These methods can be used to look for metabolites in bile (vertebrates) and aromatics in tissues (invertebrates).

In responding to PAH contamination to determine its impact on fish and invertebrate resources, it is critical to ask and answer a series of questions, such as "What is the chemical composition of the source?" "What is the fate and toxicity of the source?" and "What are the resources at risk?" In conducting analyses, it is often most appropriate to take a tiered approach that uses both screening methods and detailed analyses. Screening methods are rapid, cost-effective, provide a semi-quantitative estimate of contamination, and allow priority selection of a subset of samples for detailed analysis. Detailed analyses provide confirmation of screening results and quantitative information about individual contaminants. A tiered approach enables rapid processing of a high volume of samples, which is critical during oil spills where information about impacts to fisheries is needed quickly.

During the *Exxon Valdez* oil spill, NOAA scientists sampled a variety of fish and invertebrate species and compared PAH levels in edible tissues to a nearby, non-impacted reference site. Scientists then used screening methods to analyze metabolites in pink salmon bile in several Alaska villages where seafood safety was a particular concern; they found that metabolites in pink salmon bile were considerably higher than the reference value, but that concentrations of

PAHs in edible tissues were close to reference values. In contrast, PAHs in edible tissues of mussels, butter clams, and littleneck clams were highly elevated compared to reference values. This information was quickly relayed to fish and shellfish consumers, helping to minimize economic and subsistence impacts.

PAHs appear to be increasing in many areas where population levels are increasing. From a seafood safety standpoint, PAHs are a concern for invertebrates, but not fish. From a biological effects standpoint, however, PAHs are a concern for both invertebrates and fish. Reducing the input of PAHs into the environment and continued monitoring of PAH effects on fish and invertebrate reproduction, growth, and survival are critical to ensuring sustainability and health of the nation's fishery resources.

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VII. State and Tribal Approaches to Advisories

Setting Statewide Advisories based on Upper Percentile Lake Averages. Eric Frohmberg, Maine Bureau of Health

A key issue for developing advisories in Maine is that there are more than 3,000 lakes and ponds, and the state does not have the resources to sample them all. The question becomes, how can we develop advisories based on limited sampling data, and what kind of statistics should we use to evaluate the data we do have?

Two options are to use a mean concentration for contaminants in fish or to use an upper percentile estimate. The mean lake concentration gives you a good average population weighted exposure. This might make sense if you are addressing people who fish at different lakes in a somewhat random way. However, we don't think this is how people behave.

An upper percentile estimate of lake concentrations reflects uncertainty. We have many lakes in Maine and limited data. More importantly, it matches our hypothesis for how people fish. Many people have summer cabins and fish at a particular lake. Hence, we are concerned about someone on a high mercury lake, eating fish exclusively from that lake. Using the average value from a lake at an upper percentile, while over protective for many lakes, will protect people eating fish from these high mercury lakes.

The best data source of data about contaminants in fish in Maine is REMAP, an EPA-funded study conducted in 1993 of a random sample of 120 lakes. It looked at many parameters, including mercury. Based on the results from this sampling program, the first advisory was developed and a second monitoring program (SWAT) was established. SWAT provided data for 80 more lakes between 1994 and the present.

We have looked at the distribution of mercury values for various species across lakes. Our objective is to develop distributions of species-specific lake average mercury concentrations for 50 lakes per species. This will give us reasonable confidence in the upper percentile estimates of mercury concentration by species. The mean values for lakes average vary from about 0.3 to 0.7 ppm.

Maine has two-tiered advisories, for the general population and sensitive populations. For each species, we look at the percentage of lakes above the action level. The sensitive population action level for one meal per month is 0.8 ppm. We use this as an action level because if you cannot eat one meal per month for a non-cancer pollutant, we advise people not to eat any. If 95% of the lakes are below an action level, we do not issue an advisory.

The percentage of lakes above an action level varies. For brook trout, we found no values above the action level of 0.8 ppm. For landlocked salmon, a few lakes were above the action level. For white perch, smallmouth bass, and chain pickerel, a significant percentage of lakes were above the action level. The advisory recommends that pregnant and nursing women, women who may become pregnant, and children under eight limit their consumption of brook trout and landlocked salmon to one meal per month and that these groups eat no other fresh water fish from Maine.

For all populations, one meal per week of brook trout and landlocked salmon and two meals per month of other species are recommended limits in the safe eating guidelines.

This approach reflects our understanding of exposure. It reflects uncertainty. It provides an incentive for additional testing, as more data could lead to a better understanding of distribution. The principal disadvantage is that it is over protective for the vast majority of lakes.

Use of Maine's Statewide Advisory in a Tribal Setting. Susan M. Peterson, Aroostook Band of Micmacs

The Aroostook Band of Micmacs is the only band of Micmacs in the US. There are about 8500 enrolled members. The tribe owns about 1000 acres in Maine and additional acres in Canada and is acquiring land. The tribe does not own the lakes in which their members fish.

The State of Maine's fish consumption warnings are included in the state's book of fishing regulations. The tribe was concerned that tribal members would not read the warnings. The tribe adopted the advisories and issued its own publication called Keeping Our Traditions and Our Families Alive. It includes the advisories for freshwater and salt water fish, as well as tribe and agency contact information. It also includes guidelines for how to select, clean, and cook fish.

The Tribe adopted the Maine advisory not because they feel it is fully protective but because they do not have enough data to adopt something more protective. The meal size consumed by tribal members is probably higher than that used to develop the advisory.

The Tribe plans to develop its own advisory and to research how advisories are perceived. One approach may involve anthropological research combined with elements of a consumption survey. This would look at what was consumed in the past, what is consumed now, and whether advisories have had any effect. This would be done through interviews with tribal elders. They will also evaluate particular risks for tribal members, including increased caloric demands or increased respiration, as well as possible genetic susceptibility. This will be done in cooperation with state and federal counterparts.

North Dakota's Fish Consumption Advisory: Based on Average Concentration. Michael Ell, North Dakota Department of Health

This presentation will describe North Dakota's experience in developing fish advisories based on average concentrations of contaminants in fish.

Fish were first collected for analysis of mercury concentrations in 1991, with a focus on Devils Lake. An advisory was issued that summer. In the spring of 1992, the state issued a broader advisory, which included ten lakes and reservoirs and two rivers.

Sampling has continued since that time, reaching a peak in the mid 1990s, when more than 30 lakes and 20 species of fish were included. In the late 1990s, the state was not able to collect fish for as many lakes, so several lakes were de-listed due to lack of data and an analysis suggesting that bioaccumulation was decreasing. The focus changed to particular lakes with a lot of fishing.

In January 2001, the state issued the first statewide advisory, which remains in effect. The rationale for the advisory was that mercury occurs in all lakes, reservoirs, rivers and streams in the state. For advice to be useful, it has to be simple. The earlier advisories had 20 species of fish and 30 water bodies and were too complicated. The new statewide advisory was based on

existing data and standard assumptions. It used a reference dose of $0.1~\mu g/kg/d$ for sensitive populations.

We pooled all data available and looked at the relationship between length of fish and mercury concentration. The relationship varied between lakes. We also look at the curve to select the appropriate fish size for the statewide advisory. The lengths were converted into three categories – small, medium, and large.

NORTH DAKOTA ADVISORY FOR HUMAN CONSUMPTION OF FISH

The chart applies to fisheries of the state; data for crappie, trout and white sucker are incomplete, and the fish in many lakes, reservoirs and rivers have not been sampled. It does not consider other human exposures of methylmercury (as mercury), such as eating ocean or other inland fish.

Meal frequencies: none -- no consumption advised

occasional -- occasional consumption, 1 to 2 meals per month, avoid eating whoppers

moderate -- moderate consumption, 2 to 4 meals per month frequent -- frequent consumption, 4 to 8 meals per month

Summary: "children 5 & younger," pregnant women and nursing women can occasionally eat only smaller fish; and children over age 5 and all other adults can frequently eat smaller fish while limiting the meals of medium and larger fish.

				Fish Size		
Fish Species		Smaller	ог	Medium	ог	Larger
BASS, largemouth	Children 5 & younger	occasional		none		none
smallmouth	Pregnant &nursing women	occasional		occasional		none
smaller sizes are less	Children over 5 & under 15	moderate		moderate		moderate
than 16 inches	All other people	frequent		moderate		moderate
BASS, white	Children 5 & younger	occasional		none		none
smaller sizes are less	Pregnant & nursing women	moderate		moderate		occasional
than 12 inches	Children over 5 & under 15	frequent		moderate		occasional
	All other people	frequent		moderate		moderate
CHINOOK SALMON	Children 5 & younger	moderate		occasional		occasional
smaller sizes are less	Pregnant & nursing women	moderate		moderate		occasional
than 19 inches	Children over 5 & under 15	frequent		moderate		moderate
	All other people	frequent		frequent		moderate
NORTHERN PIKE	Children 5 & younger	moderate		occasional		occasional
smaller sizes are less	Pregnant & nursing women	moderate		moderate		occasional
than 28 inches	Children over 5 & under 15	frequent		moderate		occasional
	All other people	frequent		moderate		moderate
WALLEYE	Children 5 & younger	moderate		occasional		occasional
CHANNEL CATFISH	Pregnant & nursing women	moderate		moderate		occasional
smaller sizes are less	Children over 5 & under 15	frequent		moderate		moderate
than 22 inches	All other people	frequent		moderate		moderate
YELLOW PERCH	Children 5 & younger	moderate		moderate		occasional
smaller sizes are less	Pregnant & nursing women	moderate		moderate		occasional
than 11 inches	Children over 5 & under 15	frequent		moderate		moderate
	All other people	frequent		frequent		frequent

The reason to use the mean concentrations to develop a statewide advisory is that we are using individual fish concentrations rather than lake averages. These are composite data. It also provides more flexibility to the consuming public by giving people more opportunity to keep and eat fish. We conclude that this provides an adequate level of protection and that 75% of fish will be below the consumption level anyway. By contrast, the 95th percentile would recommend that people only consume walleye of 13 inches or smaller.

*Mercury Advisories in the State of Pennsylvania.*Bob Frey, State of Pennsylvania

The presentation will address the development of site specific advisories and a statewide advisory for mercury.

In April 2001, Pennsylvania issued a large number of site and species specific mercury advisories. The technical group had wanted to issue advisories before that but was asked by the management to wait until the release of the National Academy of Sciences analysis of the EPA RfD. They used the EPA RfD and meal-specific advisory groups based on EPA's fact sheet (EPA 823-F99-016, September 1999) but adjusted the trigger levels a bit. They issued nearly 80 new advisories.

The advisory triggers used were modified slightly from those recommended by EPA, as shown in this table:

Category of Advice	Pennsylvania (Hg ppm)	US EPA (Hg ppm)
Unrestricted	0 - 0.12	> 0.08 - 0.12*
One meal per month	0.13 - 0.25	> 0.12 - 0.24
Two meals per month	0.26 - 0.50	> 0.32 - 0.48
One meal per month	0.51 - 1.0	> 0.48 - 0.97
Six meals per year	1.01 - 1.9	> 0.97 - 1.9
Do not eat	> 1.9	> 1.0

^{*} Eight meals per month

The distribution of mercury concentrations by the advisory type is shown in this table, which summarizes ten years of data and 551 mercury data points.

Category of Advice	Number	Percent of samples
Unrestricted	222	40
One meal per month	169	31
Two meals per month	118	21
One meal per month	37	7
Six meals per year	5	> 1
Do not eat	0	0

Values for key species were walleye (n = 44) 0.069 to 1.56 ppm; largemouth bass (n = 54) 0.078 to 0.99 ppm; smallmouth bass (n = 97) 0.06 to 0.73 ppm; brown trout (n = 75) 0.007 to 0.86 ppm; carp (n = 50) 0.04 to 0.58 ppm; and channel catfish (n = 37) 0.027 to 0.78 ppm.

Species fell out differently into advisory groups. Walleye had 7% unrestricted; 30% one meal per week; 41% two meals per month; 11% one meal per month; 5% six meals per year; none at do not eat. Substantially more largemouth and smallmouth bass were in the unrestricted category.

The state also issued a statewide advisory recommending consumption of no more than one meal per week of recreationally caught sport fish, in response to questions from anglers who asked about water bodies and species not covered in the site specific advisories. The reasons include the fact that many waters and species are not tested and there could be additional contaminants.

As a result of this, they no longer issue site specific one meal per week advice.

The Total Maximum Daily Load (TMDL) regulations have implications in Pennsylvania. The state has listed water bodies with advisories on the 303(d) of impaired water bodies, which puts them in line for a TMDL. Things changed when they issued the statewide advisory, as they had eliminated one of the advisory categories. How to handle a statewide advisory for 303(d) purposes is an important question. Any place with actual fish tissue data that would result in an advisory should be listed for 303(d) purposes. Once you have a statewide advisory, you have two options. You could list only water bodies with an advisory of two meals per month (or more restrictive advice.) A second option would be to include waters where actual data fall into the one meal per week group. There are varying opinions about the best option, but the 303(d) list was recently submitted, and we will see how this falls out.

Minnesota Statewide Fish Consumption Advice. Pat McCann, Minnesota Department of Health

Minnesota is famous for being the land of 10,000 fish advisories.

We now have a statewide advisory, but also still issue site specific advice.

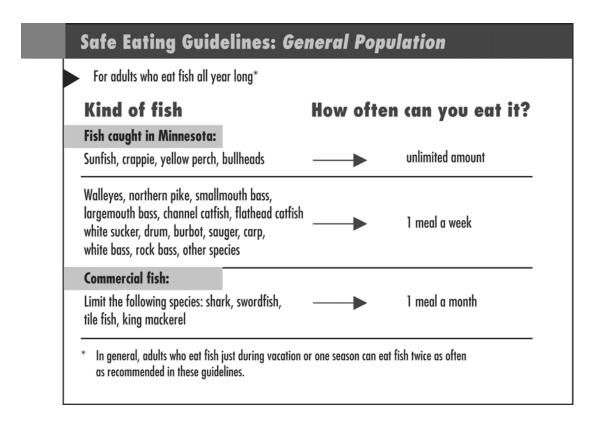
The reasons to issue a statewide advisory were because, while the state cannot test every species and every water body, we observe that every fish we do test has some mercury in it. Because of the widespread mercury, we have concluded that some advice should be available for every water body. Previously, some had the misconception that all of the water bodies on the advisory list were bad, while everything else was clean. This is not true. It is important to have advice that applies everywhere, particularly for sensitive populations. This will also simplify communication to the public.

A key question is whether the available data can be used to predict mercury concentrations in untested water bodies. We have concluded that they can be, in a general sense, though not in a rigorous sense. There is high variability in production of methyl mercury between water bodies for reasons that are not well understood. Our sampling is not designed for predictive purposes, and there are issues of selection bias and sample type consistency.

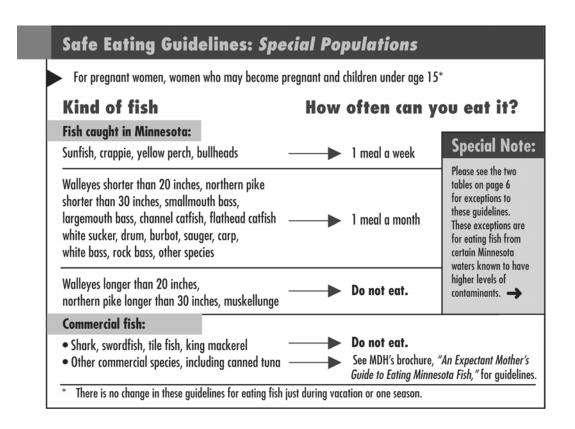
The approach used to develop advisories is a "weight of evidence" approach. We analyze data by species and geographic location, look at harvest rates, and get input from other agencies. Consistency with nearby states is also a consideration.

In 2001, we developed a new brochure to communicate a simple message and provide statewide advice. We hoped it would help people decide whether they were at risk and needed more detailed information.

For the general population, consumption is unlimited for panfish fish caught in Minnesota for (sunfish, crappie, perch and bullheads.) For all other fish, the recommended limit is one meal per week.



For sensitive populations, the panfish meal limit is now one per week; for most fish, one meal per month; for walleyes over 20 inches and some others we recommend no consumption.



The materials also show waters with more restrictive advice.

Other agencies provided input. The Department of Natural Resources wanted to continue to provide site specific advice and point out less contaminated water bodies. They were concerned about developing lists of "bad" waters. Future funding for monitoring became a problem, as money was cut from the budget due to the statewide advisory. The pollution control agency has concerns about implications for the TMDL listing process. They had listed any lake or water body with an advisory. Now they use a cutoff of 0.2 ppm. They were also concerned about future monitoring funding. Statewide advice fell more in line with their work on trends. The tourism agency was concerned about impacts on tourism.

The meal advice categories for women and children for mercury provide for unlimited consumption at less than 0.05 ppm; one meal per week from 0.06 to 0.2 ppm; one meal per month from 0.21 to 1.0 ppm; and no consumption above 1.0 ppm.

There are more than 3,500 data points for mercury in fish in Minnesota. We looked at means, which do not differ that much from the upper 95% confidence interval. Both are in the same advice category. We decided to do a length cutoff because otherwise many waters would be on the do not eat list. We also wanted to emphasize that bigger fish tend to be more contaminated. A regression analysis did not help pick a cutoff.

Communication strategies for the general statewide advice include a brochure called "Eat Fish Often," a guide for mothers, on-line resources, and a page in the fishing regulations. Site specific advice is provided on the agency web site and on DNR lake reports.

Regional Fish Advisory for the Mississippi Delta. Henry Folmar, Mississippi Department of Environmental Quality

The Mississippi Delta is very southern but also different from the rest of the south. It is highly productive but has low biological diversity. People have a deep and abiding respect for the Mississippi River. Fishing is an important part of life, and most people eat what they catch.

DDT is not a new problem in the Delta. It was heavily used after World War II. It lasts a long time, even though banned in 1972. Use of DDT led to the decline in fish eating species like the bald eagle and brown pelican. Fish advisories were issued for certain Delta lakes in the 1970s.

Recent studies show that the Mississippi has some of the highest DDT levels in the country. Whole carp had the highest levels of any 112 sites monitored by the US Geological Survey. Yazoo Refuge was closed to fishing due to DDT. Levels were also found to be extremely elevated in the delta.

Levels of DDT in fish are declining. Data show a three-fold decline since 1984 at the Yazoo River at Redwood Mississippi in both DDT and toxaphene. Some data show a greater decrease since the 1970s.

Concerns remain because the levels considered to be safe have also changed. The Food and Drug Administration rescinded its action level in 1993. States were encouraged to use guidance from US EPA that was more protective.

The Mississippi Fish Advisory Task Force developed new criteria for DDT and toxaphene in fish. The task force included several agencies, followed EPA guidance and also sought advice from experts from outside the government. The criteria are shown in this table.

Mississippi Fish Advisory Criteria for DDT and Toxaphene

Consumption Advice	Fish Concentration of DDT in ppm	Fish Concentration of Toxaphene in ppm
No limit	< 1.0	< 0.4
Two meals per month	1.0 to 5.9	0.4 to 1.9
No consumption	≥ 6.0	≥ 2.0

A Mississippi Delta fish tissue study was conducted to evaluate DDT and toxaphene in edible fish tissue at ten sampling sites. These data were used to evaluate human health risks and to develop an approach to future monitoring.

The study was conducted in 2000. All largemouth bass, bream, crappie, freshwater drum and all catfish less than 3 pounds were below the criteria. 66% of samples were below the criterion for DDT; 73% for toxaphene. Farm raised catfish were below the criteria for both pollutants.

All ten sites had at least two samples above the consumption criteria. Some form of advisory was warranted at each site.

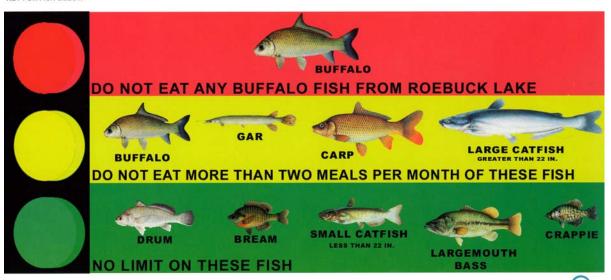
The group developed Mississippi's first regional advisory. For buffalo, gar, carp, and catfish over 22 inches, recommended consumption was two meals per month. No limit was adopted for drum, bream, small catfish, largemouth bass, and crappie.

The advisory applies to the Delta from Memphis to Vicksburg but not to the Mississippi River or oxbow lakes connected to the river.

In addition, for one lake, Roebuck Lake, they recommended no consumption of buffalo. The Mississippi Department of Wildlife Fisheries and Parks also issued a commercial fishing ban for Roebuck Lake.

DELTA FISH ADVISORY

KEY FOR FISH BELOW



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There was a public media campaign that included news conferences, new releases, staged sampling demonstration photo-ops, radio and TV spots on morning shows, call in shows on gospel and blues radio stations, distribution of letters and posters to stores, door to door canvassing in some communities, and signs at boat ramps. Letters and brochures were mailed to 1400 churches; 16,000 coloring books were distributed; and posters and brochures were placed at WIC offices. The materials were also translated into Spanish.

Next steps are to continue monitoring for both hot spots and areas that can be removed from the advisory, to continue outreach efforts, and to develop TMDLs.

Advisories Based on Eight Meals per Month. Joe Beaman, Maryland Department of the Environment

Maryland provides guidance for three populations: the general population, women of child-bearing age, and young children. The state uses three meal sizes (eight ounces for the general population; six ounces for women; and three ounces for children to age six).

Advisory recommendations are provided for the following consumption rates: less than 1 meal per month (4-11 meals per year), 1 meal per month, 2 meals per month, 4 meals per month, and 8 meals per month. The decision to provide recommendations for up to 8 meals per month was a policy decision focused on protecting frequent fish consumer groups based on anecdotal knowledge about these populations in Baltimore City, urban Maryland near the Potomac, and the Eastern Shore. It was not based on a formal exposure assessment.

What does eight meals per month mean?

For carcinogens (PCBs for example), the resulting threshold ranges are 20 to 39 ppb for general population and 17 to 33 ppb for women of child-bearing age. This corresponds to a 1 per 10,000 risk level. Maryland assumes 30% cooking loss for carcinogenic compounds.

For non-carcinogens (methyl mercury), the threshold for eight meals per month are 59 to 117 ppb for the general population, 54 to 107 ppb for women of child bearing age; 13 to 26 ppb of PCBs for children to age six; and 32 to 64 ppb of mercury for children to age six. This is based on an RfD of $0.1 \,\mu g/kg/d$ for mercury and 0.05 for PCBs.

Decision rules establishing data sufficiency thresholds state that an advisory may be developed for a minimum of 5 fish. Decision rules for temporal relevance allowed data from 1995 - 2001 to be used to establish advisories released in 2001.

The data supporting the statewide mercury advisories came from the Department of Natural Resources, which sampled 20 lakes of 80 acres or more. Maryland has about 372 lakes or impoundments. Species collected were largemouth bass, smallmouth bass, bluegill, sunfish, and black crappie. About 59% of the lakes greater than 50 acres had sufficient data for advisories for bass, bluegill and/or crappie. For each species, a geometric mean was calculated for each lake and then the average of the geometric means for the lakes was used as the threshold to set the advisory. Three lakes had higher values than all others and were separated out and given special advisories.

PCBs advisories for eight meals a month were issued for white perch for rivers on the lower Eastern Shore, including the Choptank, Nanticoke, and Pocomoke. The average PCB level in these tidal tributaries was 27 ppb.

The advantage of issuing an advisory based on consumption of eight meals per month is that it provides information to fish consumers including low-level subsistence users about locations and species of fish that can be consumed frequently (2 times per week) without concern about health effects. The disadvantage is that any advisory may discourage fish consumption, even of relatively clean fish.

A key outstanding issue is that data on exposure are lacking. The state is currently conducing mail surveys among licensed anglers and interviews in urban areas. They will use this information in tailoring the advisory recommendations to the populations of concern based on their specific consumption habits.

Bob Brodberg: question for Henry Folmar on the risk communication. What did this cost?

Henry Folmar: I don't know. There was no budget for it, and we just bootlegged it out of other programs. We have not put a pencil to this.

Bob Brodberg: Did you look at mercury?

Henry Folmar: We did not look at mercury in these fish but have not previously found mercury in the fish. Sediment conditions do not appear to be favorable to methylation.

Andy Smith: Tell us what sort of mercury levels you have seen? I am also very impressed with the risk communication program. Are you doing any assessment or evaluation?

Henry Folmar: For mercury, they are still using an action level of 1 ppm. The levels they are seeing in largemouth bass are around 0.2 or 0.3. As far as outreach, there is nothing on the books to target evaluation. There is a guy who is doing a consumption survey and they are going to try to persuade him to repeat it.

Andy Smith: How did you actually develop materials? Did you use focus groups?

Henry Folmar: We did not officially call it a focus group but had citizen input from people on the Delta.

Question: I want to turn Andy's question back to him. What is the response in Maine to the advisories in general? Are people following them?

Eric Frohmberg: We do have a follow up program to look at awareness of advisories. Henry presented some of the data yesterday. It is better than it used to be and not what we wish it would be.

Sue Peterson: We have not received any feedback as yet. We may develop a video and use tribal language.

Andy Smith: We will be getting data from pregnant women including hair mercury and survey information. For the general population the advice is not that restrictive. We have some data on angler behavior. Most anglers are not eating enough to be affected by advisory in the first place.

Question: Remember the presentation on PAHs off the coast of Alaska. The salmon there that were smoked were much higher than salmon from oil spill site. Are you thinking about putting advice about smoking in advisories?

Sue Peterson: We could consider that in the future.

Jeff Bigler: I don't recall that there was risk information presented. It might be worth looking at risk.

John Persell: We could look at this. But remember that native people have been smoking fish for generations.

Bob Brodberg: In Maine, do you sample marine waters at all? How does this match up with statewide advice?

Eric Frohmberg: We do look at marine waters and shellfish. The big marine species that have been a problem are bluefish and striped bass. Our striped bass and bluefish advisories, however, are driven by PCBs, not mercury.

VIII. Approaches to Considering Benefits in Advisory Programs

Perspectives on Considering Risks from Contaminants in Fish. John Persell, Minnesota Chippewa Tribe Research Lab

People like good news better than bad news. For high end consumers, people are paying attention to the message that fish is good food.

People may reserve judgment about information they hear. Think of cigarettes and smoking. Science told us that all of those toxics in the body were bad for us, but there were also scientists on the other side that kept things from advancing.

Working with Indian people, the feedback is that they don't trust what we say as scientists, and they will make their judgments based on what they feel is best for them. Our credibility and our ability to communicate results are key. We can do the best science in the world, but if we can't communicate it then we are spinning our wheels. One of the major goals that I have set out is to shine light on the information that we have. Let's communicate risk as best we can. I am pleased to see the outstanding message development presented by the gentleman from Mississippi.

Let's also consider how we got to where we are today and how we can fix the problem. I never go to a meeting with the tribal government to communicate risks without somebody saying, what are we doing about this? The Minnesota Chippewa tribe wants their treaty rights back. They want to be able to eat these resources at a level that would sustain them.

Three years ago the tribe embarked on a project to determine contaminants in nature's food sources and alternatives. They had been measuring contaminants in fish since about 1992. They developed guidance for what might be safely consumed for three groups: women and children, 50 kg adults; 70 kg adults. They have been looking lake by lake and looking at multiple species, trying to inform their decision making process. They are also looking at risk assessment process itself including the assumptions made. Do we consider all contaminants? What about those we are not aware of? If we have information on particular contaminants, that is the easy part. What about those we have no information for? Maybe we need to include a factor for these. Do we consider multiple contaminants? What about endocrine disrupters? Cancer is not the only endpoint of concern.

Fish is good food. It has cultural and spiritual values. It helps to keep culture alive. What does it do to the human spirit when we know that fish is contaminated? What are the ethical concerns? If fish is a gift of the creator, then what does it mean if it is contaminated? What does it mean to people who think that they are the protectors?

We need to consider additional species. It may be important to look at moose, grouse and rabbits. We are looking at wild rice. Dioxin has been found at 0.6 pg/g in rice kernels. In a year or two, the tribe expects to publish their first comprehensive food guidance addressing all food sources including grocery stores and commodity foods. They are going to do some local testing and look at patterns. They want to be accurate with what they are going to put out in guidance. They will be supporting a health and well being paradigm. The hope is that in the future we will be looking at this in a different way and look at restoration of the resource.

*Impacts of Fish Contamination on the Columbia River Basin.*Paul Lumley, Yakama Tribe

The Columbia River basin is large. There are four member tribes of the Columbia River Inter Tribal Fish Commission (CRITFC) – the Nez Perce, Umatilla, Warm Springs, and Yakama. There are a total of 14 tribes in the Columbia River basin.

The purpose of the study was to evaluate the likelihood that Native American tribal members may be exposed to high levels of contaminants from eating Columbia River Basin fish.

The first phase was a fish consumption survey, and the second phase a fish contamination study.

The fish consumption survey investigated two questions: are tribal members eating more fish than average and are they being protected by water quality standards based on a national fish consumption rate of 6.5 grams per day?

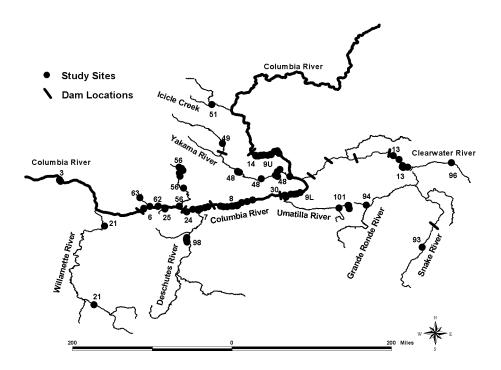
Fish species identified as important for the basin include salmon, rainbow trout, mountain whitefish, eulachon, lamprey, walleye, white sturgeon, and largescale sucker. A hypothetical diet was constructed with these species. The fish consumption survey found tribal members with average consumption rates ate two meals per week and those with high consumption rates ate 12 meals per week. Tribal member eat about nine times the amount of the general public. Children eat about three times the national average. Adults eat 58.7 grams per day on average. They are probably not protected by the water quality standards based on lower rates.

The goals of the fish contamination study were to determine whether fish were contaminated, whether there were differences in concentrations between species and locations, and whether tribal members face a higher risk. The study was not designed to evaluate people's health, intergenerational risks, rates of disease, or sources of chemicals.

The study sites were not random and were mostly on the Columbia River main stem at places where tribal members catch fish. 300 samples were obtained from tribal fishers and hatcheries, with three replicates per site. The resident species included white sturgeon, mountain whitefish, rainbow trout, walleye, bridgelip, and largescale sucker. Some are commercial species. The anadromous species included Chinook salmon, coho salmon, steelhead, eulachon (smelt), and Pacific lamprey. Samples were analyzed in various ways because people eat fish in various ways. The samples were analyzed for 132 chemicals.

The resident fish were found to have considerably higher concentrations of many contaminants than the anadromous fish. For aroclors, resident fish were higher, but Pacific lampreys also showed 100 ppb. Mercury showed up in both at similar amounts.

The total cancer risk was calculated to be 4×10^{-4} for tribal members. This is for the average consumer. Some are higher consumers. The pollutants contributing the greatest risk varied by species, though PCBs, mercury, dioxins, DDT, and arsenic seemed to be most important overall. The hazard index for non-cancer effects was above three, when hazard indices for all types of effects were added.



The most contaminated fish were found in upper parts of the basin. There is some contamination from Lake Roosevelt. They will be bringing in more tribes to discuss these results.

The conclusions of the study were that the fish were contaminated; that there are differences between species and locations, and that tribal members are exposed to a higher risk. Tribal members eat a lot more salmon (anadromous species) than resident fish.

US EPA has concluded that the Columbia River basin results are similar to other large river basins in the US in terms of contamination. Industrial groups seem to be honing in on this as a reason to avoid addressing the critical issues. This is a significant issue for the Columbia River tribes.

The four member tribes do not have advisories. The report received considerable news coverage. If they issued fish advisories, they would have to be careful and be scientifically credible.

Some of the issues to consider include the following.

Salmon is very important from a cultural perspective. It is the first food placed on the table at a long house ceremony.

The tribes have treaty rights. Treaties of 1885 guarantee the "right of taking fish at all usual and accustomed places." They take this very seriously. Some sites have been covered up by the dams. The Columbia River basin used to produce more salmon than any other basin in the world, and now it produces more electricity. When the tribes signed the treaties they never envisioned the fish would become toxic

The organization's primary mission is to restore the fisheries, not human health. The tribes are struggling with the report because they are trying to get people to return to a traditional diet

because of other health problems. People are demanding answers from leaders about cleaning up contaminants. People see health as embodying physical, mental, spiritual, and cultural qualities.

Fish preparation methods may be an important issue. Canning has become more popular. Drying salmon is healthier. They are advising people go to back to the more traditional ways. Some traditional methods may not be healthy, however, such as whole fish soup and eating salmon eggs.

There are issues about the health of the fish. Research needs are significant and include pathology, toxicology, etc. The tribes do not have staffing to address fish health. Fish health issues tend to get lost in the shuffle compared to human health. There is a need for more discussion of stewardship of the fish. It is difficult for tribes to do it as well, but we need to consider this.

The economic benefits of the fish in the Columbia River Basin are substantial, amounting to about \$2 million for tribal members annually. The tribes are looking at ways to add value to product by smoking, etc. The recent EPA report has impacted tribal ability to market salmon. Farmed fish may be ten times more toxic than wild fish.

Environmental cleanup is important. There are a lot of legal and political issues. The agricultural industry is large. Cleanup would take a major effort. Environmental justice is a concern. Risk assessments need to be done by and for the tribes, but they do not have the staff within their governments to do this at present. There are limitations to tribes addressing these issues. Understanding and communicating results to tribal members are important. EPA is not planning to use report to advise the general public. The tribes have to address it. They are initiating an effort to coordinate tribal efforts.

The tribes do not want to see another study presented to them. They want to see something done about it. The next step is to look at action to clean up the environment.

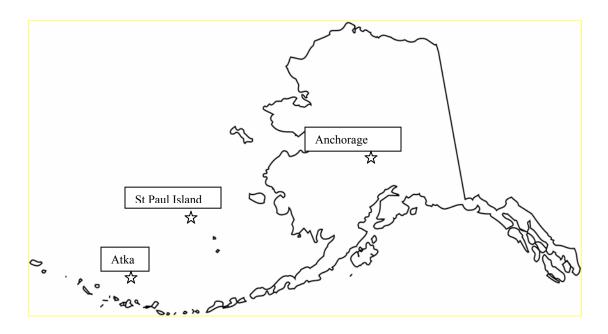
Dietary Benefits and Risks in Alaskan Villages. Suanne Unger, Aleutian/Pribilof Islands Association

The focus of the project is on community health issues and community services. There are community-based coordinators in the villages involved in the study.

There are more than 229 tribes in Alaska. In rural Alaska, the subsistence harvest is about 375 pounds of fish, marine and terrestrial mammals per person per year, compared to an average US annual consumption of 255 total pounds of meat, fish, and poultry.

In Alaska, the main subsistence food is fish, at about 65%. Common species are salmon, halibut, herring, whitefish, cod, and Dolly Varden. Subsistence is very important in Alaska. It is not just to supplement the diet.

In the Aleutian/Pribilof region, at St Paul Island, subsistence harvest and use of marine mammals is almost equal to that of fish. The percentage of households that use marine mammals varies among communities, though the highest rates are at Atka, Nikolski, and Akutan, at more than 90%.



The purpose of the study is to encourage healthy dietary choices by raising awareness about the rural diet and the risks and benefits unique to foods consumed at Atka and St. Paul. There are a lot of unique situations in rural Alaska with regard to risks and benefits. The intention is to produce a process that other tribes can replicate.

There is currently no consumption advisory in Alaska except that unlimited consumption is recommended by the state health department due to benefits. This is a confusing message to people. People are concerned about increasing cancer and increasing blights and sores that they observe on fish. Part of the purpose is to help tribes recognize they can start to monitor local species and work at the community level.

Key questions that people have are: Is traditional food safe to eat? What are benefits and risks of traditional foods? What are the benefits and risks of changing from a traditional diet to a more store-bought diet?

The community goal is to restore and maintain healthy lifestyles and cultural connections for this and future generations and to achieve holistic community health in Atka and St. Paul. This is defined as a natural interplay among cultural, physical, environmental, economic, spiritual, social, and emotional forces.

The hypotheses of the study are that: traditional foods are safe to eat and are an important part of a nutritious balanced diet; maintenance of a traditional diet enhances community cohesion, cultural connection and community and individual health; increasing substitution of traditional foods with commercial foods in the diet is resulting in negative health effects; many factors are influencing the collection, use and benefits of traditional foods.

The two communities were chosen for the study because they have high use of subsistence foods and are far removed from the urban center of Anchorage. Foods are expensive and there are limited choices for fresh foods. In St. Paul, testing has shows high levels of persistent organic pollutants in northern fur seals; people have had dramatic changes in their diet; there is a high

rate of diabetes; and there is access to store bought foods. In Atka, some studies have also shown persistent organic pollutants, and the community is in close proximity to Amchitka Island.

Tracey Lynn Alaska Division of Public Health: The presentation made reference to a POPs study that has been conducted in parts of Alaska. It was not a random sample as they tried to encourage certain people to participate.

Question: How do you {tribes} like to be approached by researchers? Particularly one who has never worked with a community before?

Paul Lumley: The best way to work with a tribe is to develop a relationship with someone in the tribe. Each tribal government has a different structure.

Marvin Kline, Fort McPoint Environmental Department: Tribes are at a crossroads. I don't think that going back to traditional ways will help to deal with more powerful culture that we see on TV. Advisories are necessary for elders and for those who want to practice subsistence. For people like me, who decide to be more assimilated, what kind of curriculum are you offering or are you encouraging youth to go to college for natural resources management, etc.

Paul Lumley: A lot of members are focused on cultural practices. In our reservations, the economic conditions are pretty bad, and there is a lot of apathy. It is important to be careful about recommendations to cut back on the use of salmon. You can also make advisories but that does not mean people have to abide by them. High consumers may not change. I will not ask them to reduce salmon use. We need to give them information. If it is true that fish is contaminated, we need to let them know.

Sue Unger: One thing we are hoping to do is to get students involved in parts of the analysis per the laboratory.

John Persell: The tribe has a critical professions program to encourage people to get into critical training.

IX. Looking at Health Benefits of Consuming Fish

Overview of Benefits of Fish Consumption. Judy Sheeshka, University of Guelph

Consumption of fish has health benefits that depend on the amount consumed, species, and what foods are replaced by fish.

Fish are a good food source because they have high quality protein, "good" fatty acids, and vitamins and minerals. Good quality proteins are those that have all of the essential amino acids and are available to the body. The proteins in animal foods have all nine amino acids, while plant foods do not. This is why vegans need to be careful about combining their plant sources to gain all of the acids. Egg proteins have the highest quality, followed by fish. Sometimes what appear to be big differences in quality disappear when you look at the actual diet. Substituting chicken for fish produces fairly similar result while substituting hot dogs results in what dieticians would consider to be a disaster because of much higher fat concentrations.

Current dietary guidelines recommend 25 to 35% of calories from fat. This is based on benefits of a Mediterranean style diet, with emphasis on low saturated fats. Saturated fats come from meats, baked goods, and high fat dairy products and tend to raise the "bad" cholesterol. Mono and poly unsaturated fats (MUFA and PUFA), in fish, vegetable oils, and nuts, are considered to be good fats. They lower serum LDL (bad cholesterol) and raise HDL (good cholesterol), which lowers the risk of heart disease.

Both lean fish and fatty fish have 75% heart healthy fat. On average, only 25% of fat in fish is the bad kind, compared to 40% in beef. This is pretty consistent across species.

Omega 3 fatty acids are a form of PUFA found in fish and nuts. The two of greatest interest are DHA and EPA. They are not only found in all fish, though the amounts are less in lean fish. The amount of these acids in fish depends on the temperature of the water where the fish live. Examples of amounts found in different types of fish are shown below.

N-3 Fatty Acids in Fish (grams per 100 grams of fish)

		EPA		DHA
Large-mouth bass		0.31		0.45
Coho salmon		0.40		0.66
Rainbow trout	0.47		0.56	
Fresh-water drum		0.29		0.37
Channel catfish		0.10		0.14
Northern pike	0.04		0.09	
Walleye		0.11		0.29
Yellow perch		0.10		0.22

Fish and mercury and fish and omega acids are another issue. Mercury does not necessarily cooccur with the beneficial fatty acids because the fatty acids go into fat not muscle. A fatty fish can be either low or high in mercury. Walleye tend to be higher in mercury while perch are low; both have high concentrations of omega 3 acids. Pike has low fatty acids and high mercury.

There is some debate about omega 3 concentrations of farmed fish. The type of feed is important. Farmed fish are higher in total fat than other fish. The percentage of omega 3 acids as a percent of total fat is lower. But the amount of omega 3 acids per gram appears to be similar as in wild fish. It depends on how data are expressed.

Omega 3 fatty acids are important to growth and development and are important during the third trimester up to twelve months of age. The mother's consumption leads to the baby's initial exposure.

There seems to be agreement that one to two fish meals per week will reduce deaths from myocardial infarctions and will also reduce all-cause mortality. The acids reduce triglycerides (which are risk factors for heart disease) in the blood but results for cholesterol are not consistent.

The literature is difficult to interpret because there are different cardiac endpoints. Mechanisms are not known. Some effects do not increase with dose. Lean fish produce the same effects as fatty fish. Addition of 1 gram per day of fatty acid supplement provides improvement but higher doses do not. The benefit plateaus at two fish meals per week. This suggests that something else at play here. Two meals per week of lean fish do not contribute much in the way of omega 3 fatty acids. The studies have only included well educated, relatively wealthy people. The American Heart Association recommends at least two fish meals a week, and the evidence clearly supports 1 to 2 fish meals per week.

There is evidence that fish consumption can protect against cancer especially in the GI tract.

Fish consumption may be beneficial for stroke. Research suggests that some kinds of stroke may be affected and others not. Adding fish to diets designed to lower blood pressure (low salt, etc), along with weight loss and exercise, reduces blood pressure.

To summarize the findings, all fish contain the omega 3 fatty acids, which are highly beneficial during pregnancy and the first year of life and which are found in all fish. The effects of fish on reducing chronic disease may be independent of the effects of fish on blood lipids (including cholesterol). There is complete consistency in the literature that says that having no fish is a health risk.

Use of Quality Adjusted Life Years to Assess Risks and Benefits of Fish Consumption. Rafael Ponce, University of Washington

The benefits and risks of fish consumption are a key concern. Benefits include high nutritional quality, often inexpensive cost, often ready access, health benefits (cardiovascular disease, neurodevelopmental), social and cultural associations. Risks include health effects of harmful environmental toxicants. There are also issues of risk substitution.

A decision problem is how to develop methods and conduct analysis when disparate health endpoints are at risk.

An ideal policy tool would allow consideration of both risks and benefits; be transparent, rigorous, and theoretically well-founded; allow consideration of uncertainties, correlations; be flexible and allow updating with new information.

The available tools include risk analysis (which compares disease incidence to identify best policy); benefit-cost analysis, (which considers whether the benefits of implementing a policy outweigh the cost); cost-effectiveness analysis (which considers which policy option has the greatest effectiveness per unit cost). In any of these analyses, you need similar "units."

Comparisons of risk are not sufficient for health policy decision making because each risk does not have the same impact or consequences. Economists try to develop ways to define when health endpoints are equivalent. Ways to determine when health endpoints are equivalent could include the following: when an individual is ambivalent between two health effects; when health effects have comparable duration; when health effects have comparable population impact.

Use of QALYs (quality adjusted life years) is suggested because it is one way to compare. They divide health impacts into two elements: duration of impact and quality of life. The method assumes that these are independent. Half a year of perfect health equals one year of half-health. This is used for evaluating therapies and screening programs, as well as disease burdens.

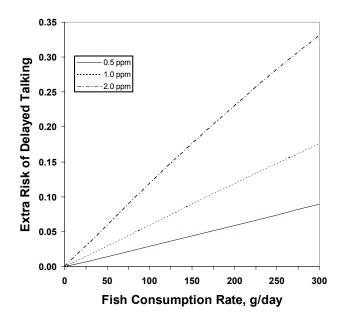
To do this, researchers assess preferences and aversions for different health states and rate them on a scale from 0 to 1, where 0 represents death and 1 represents perfect health. There is some controversy about whether this is an appropriate. Discounting is also a concern; is the value of life at 55 the same as at 23?

To estimate net benefit/risk, one can use QALYs to adjust dose-response functions. Once normalized, dose-response functions can be directly compared and then combined to get a net health impact. This allows for the comparison of endpoints that differ in risk and consequence. The method is presented in more detailed in two papers [29, 30]

This case is presented as an example. It was not intended to be definite. Although realistic data were used in the derivation of this case, it is not intended as a definitive analysis. A number of assumptions need careful consideration. It considers only a single benefit and risk endpoint. The risk is neurodevelopmental delay from prenatal MeHg exposure. The benefit is reduced risk of fatal myocardial infarction with eating fish. The populations modeled are a general population of 100,000 and a population of 100,000 women of child-bearing age and their children. A fish intake of 0 to 300 grams per day of fish was used. This includes 99th percentile of fish consumers for the lower 48 states. The concentration of methyl mercury in fish was assumed to be between 0 and 2 ppm.

To model risks they the Iraqi poisoning data [31] and a Weibull dose-response model from US EPA. They estimated the risk of neurodevelopmental delay from methyl mercury in fish, with a reduction in the quality of life decreased from on the scale from 1 to 0.9. They assumed a lifetime impact of reduced quality of life and used life table to estimate lifespan.

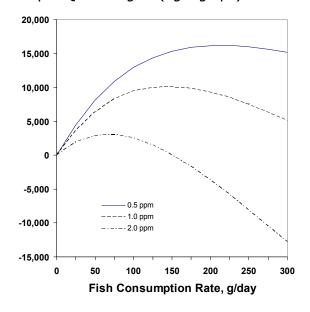
A plot of the extra risk of delayed talking against mercury consumption in fish based on this approach is shown below.

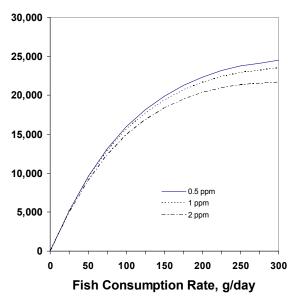


To model benefits they used CDC data to estimate lifespan using mortality rates by all causes and by MI. They estimated benefits of fish consumption [32, 33] and modified the mortality rates, assuming that the male data was applicable to females.

They aggregated risks and benefits. They assumed equivalent health impacts for the two outcomes. This is not an appropriate assumption. There is no discounting of effects. There is an ethical issue here because benefits go to adults and risks to kids. This graph shows the net health impact.

Net health impacts for 100,000 men and women with equal QALY weights (left graph) and unequal QALY weights (right graph).





The conclusion of the analysis is that, depending on the model assumptions, restrictions for the general population to limit fish consumption could do more harm than good. Recommendations to limit fish intake during pregnancy would do more good than harm.

The method is amenable to sensitivity and uncertainty analysis. It is possible to adjust the QALY weights and dose-response modeling. It is amenable to discounting; forecasting and can consider multiple benefits/risks. It requires data on health effects (dose-response, age-specific rates, duration of effects). Other issues are that extrapolation of data from animals is uncertain. It requires quality of life weights for each endpoint.

Tracey Lynn: Have you considered further developing model to take into account multiple endpoints? Look at risks and benefits for women, for example.

Response: No

What was the age definition of women and children?

Response: We used life tables; do not specify age. We only looked at the fetus and following the impact over a lifetime

On the second population there was no benefit because low risk of MI – what about benefit of future reduction of MI.

Response: We did not consider that.

Re: risk of not eating fish. What if you replace it with other good nutrition not hot dogs?

Sheeshka – Researchers concluded that a diet high in fish was healthier

Eric Frohmberg – We should be careful about how commercial fish is described across the states. King mackerel is a high mercury fish rarely seen in Maine and another form of mackerel is a poster child for low mercury.

Lynn Tracey, Alaska Division of Public Health: The State of Alaska would like to see salmon included on list of good fish.

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